

***Preliminary Remarks***

Applicants thank the Examiner for his careful consideration of their 1/13/03 Response and are appreciative that the number of open issues has diminished.

Still, Claims 1 – 46 remain rejected under 35 USC §§102 and 112 based on a number of positions laid out in detail in the 03/06/03 Office Action. Applicants respectfully disagree with the conclusions set forth in that office action. However, in order to expedite prosecution of a portion of their invention of particular current interest, Applicants have presented a set of more narrowly focused amended claims in the attached Listing of Claims. That Listing of Claims will replace all prior claims in this case.

Applicants respectfully request entry of this amendment and consideration of the attached claims and accompanying comments. The claims are now significantly fewer in number and are believed free from most of the issues discussed in the 03/06/03 Office Action. Applicants' comments address any residual issues. The attached amended claims thus reduce, if not eliminate, the number of remaining legal issues and are intended to place the case in better condition for allowance or appeal.

The deletion of any claims and any other loss of claimed subject matter is being made solely for the reasons noted above, rather than in acquiescence to any positions taken by the Examiner. In fact, applicants are *not* acquiescing to any of those positions and are submitting their amendments without prejudice to the subsequent prosecution of claims to some or all of the subject matter which might be lost by virtue of this paper.

***Additional Comments*****(A) Discussion of claim amendments**

Claims 1 – 21, 35, 37, 38 and 41 – 46 have been cancelled to focus attention on subject matter of particular current interest to applicants.

Claims 47 – 49 have been added to complete the now substantially reduced claim scope. These three new claims introduce no new matter.

- New claims 47 and 48 simply reiterate the text of previous claims 25 and 26 to eliminate multiple dependency.
- New claim 49 is supported in the specification, e.g., on page 13, line 15.

Claim 22 has been rewritten in independent form, incorporating limitations taken from now-cancelled claims 20, 19 and 9.

The dependencies of most of the claims now pending have been adjusted to reflect the cancellation of many of the previous claims.

Claim 36 had previously encompassed three subsets of compounds as defined by the three alternative sections of proviso C (see page 119, lines 25 – 35, of the application as filed). The claim has now been narrowed to focus on the subset in which R<sup>C</sup> is linked to purine ring position 2 via a carbon-carbon bond. Accordingly, the remainder of proviso C and original proviso B have been deleted as irrelevant, and the definition of R<sup>C</sup> has been limited to those moieties which can be linked by a C-C bond as required by the surviving portion of proviso C. Reiteration of the definition of R<sup>3</sup> has been fixed.

Claim 39 was amended to insert the definition of R<sup>6</sup> which is supported in the specification e.g., on page 5, lines 29 – 30, and in original claim 32.

In addition, a number of language changes were made in one or more of the claims, such as

- Changing “terminating in a cyano” to “bearing a cyano”
- Changing “pharmaceutically acceptable derivative” language to “salt” and “ester” language
- Deleting prodrug references.

**(B) Art Rejections**

The claims presented herewith are believed free of any of the cited art.

Note that none of the cited references disclose compounds which contain any of the following:

- a substituent at position 9 of the purine ring system as required by the definition of R<sup>A</sup> in claim 22 or any its dependent claims
- an aryl substituent linked directly to the amino group at position 6 of the purine ring system as required by the structures depicted in claims 36 and 39
- a carbon-carbon linked substituent at position 2 of the purine ring system as required by the definition of R<sup>C</sup> in claim 36.

**(C) Double Patenting Provisional Rejection**

Applicants remain prepared to take appropriate action, including a terminal disclaimer, to the extent that is necessitated by the ensuing prosecution of this case and copending USSN 09/740653.

**(D) Rejections Under §112, 2d Paragraph (Indefiniteness)**

Many of the issues raised in the last office action have been rendered moot by the attached claim amendments. Applicants additional comments are set forth below, retaining the numbering used in the last office action.

1, 2. Claim amendments have rendered moot the issues concerning "terminating in a cyano" and "amino acid".

3. Claim amendments have rendered moot the issue concerning Y and R<sup>1</sup>. As is clear from the definition of R<sup>1</sup>, Y can indeed be O, S, NR or a covalent bond. The prior reference to Y has been amended to be consistent with that.

4. Claim amendments have rendered moot the language issue concerning " M-M' ". Nonetheless, applicants point out that the convention of using a slash or prime to mark a subsequently

mentioned independently chosen example of a given group is reasonably clear from the specification. For instance, note on page 3, lines 26 – 28: R and R' are independently chosen from the same set of possibilities. The R' is simply noted parenthetically. A similar usage occurs on page 4, lines 16 – 18 where R<sup>J</sup> and R<sup>J'</sup> are independently chosen from the same set of possibilities. The situation is the same for R<sup>K</sup> and R<sup>K'</sup> on page 4, lines 18 – 24, where by implication, the choices for both R<sup>K</sup> and R<sup>K'</sup> must be those provided for R<sup>K</sup>. In any event, the issue is moot with respect to the claims as amended.

5 - 7. Claim amendments have rendered moot the issues concerning possible unsaturation of a string of methylene groups, the use of "pharmaceutically acceptable derivative" and the definition of R<sup>K</sup>.

8. The term, "acyl" still appears in claims 25 and 47. Its meaning is well-known in the art and not indefinite. Its meaning is at least sufficiently definite that the term is used frequently in the PTO's Manual of Classification, e.g., in definitions in Class 560. Specifically, an acyl group is the residual moiety after the -OH of a carboxylic acid has been removed. See e.g. Morrison and Boyd, "Organic Chemistry" (3d ed), page 658, copy attached.

9. Claim amendments have rendered moot the issues concerning reiteration of "sulfate, sulfonate".

10. The terms "sulfate" and "sulfonate" are understood in the art to mean a salt or ester of a -OSO<sub>3</sub>H or -SO<sub>3</sub>H substituent. See Webster's Medical Desk Dictionary (1986), page 689, copy attached. Their meaning is considered sufficiently definite in the art for use in our claims.

11. Claim amendments have rendered moot the issues concerning use of the phrase, "phosphorus-containing moiety".

12. Appropriate definitions from the application as filed have been added to claim 36.

13. The issue of the significance of the comma on line 5 of page 114 has been rendered moot by the cancellation of claim 17. However, note that the position of the comma indicates that R<sup>3</sup> is the referenced substituent for the aryl group of the alkyl-aryl or alkenyl-aryl moiety. Choices for R<sup>A</sup> are

set off from one another by semicolons, rather than commas. Again this issue is moot by virtue of the cancellation of claim 17.

14. A definition of  $R^6$  has been added to claim 39, as previously discussed.

15. The issue of the definition of R in the context of  $R^A$  and  $R^D$  in claim 17 has been rendered moot by the cancellation of claim 17. However, what was intended in claim 17 is the following: each occurrence of R is independently selected from the listed items, with the additional limitation in the case of  $R^D$  (i.e., when  $R^D$  is -YR) that the R group chosen for that context will additionally not bear a cyano, etc. We see no inconsistency or lack of clarity in that now cancelled claim.

16 and 17. Claim 36 has been amended as previously discussed. As will be seen, all occurrences of the variable R are consistent with its definition.

#### **(E) Rejections of Claims 43, 45 and 46 Under §112, 1<sup>st</sup> and 2d Paragraphs**

These rejections are rendered moot by the cancellation of the relevant claims.

#### **(F) Conclusion; Notice of Appeal**

Once again, applicants thank the examiner for his continued thorough and thoughtful review of this case. We believe that the claims as amended are in good condition for allowance. If any issues remain open which might be amenable to resolution by phone, the Examiner is invited to call applicants' undersigned attorney. Applicants' Notice of Appeal is included herewith in case appeal proves necessary.

Respectfully submitted,

David L. Bernstein

David L. Bernstein, Reg. No. 31,235  
ARIAD Pharmaceuticals, Inc.  
26 Landsdowne Street  
Cambridge, MA 02139  
phone: 617-494-0400 ext 266

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Sue Wilson